



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT(s): QIN, Yixian, et al.

EXAMINER: BOR, Helene Catherine

SERIAL NO.: 10/522,452

ART UNIT: 3768

FILED: June 20, 2005

DATE: May 13, 2007

**FOR: METHOD AND APPARATUS FOR SCANNING CONFOCAL
ACOUSTIC DIAGNOSTIC FOR BONE QUALITY**

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

**37 C.F.R. § 1.131 DECLARATION OF PRIOR INVENTION
TO OVERCOME CITED ARTICLE**

I, Yixian Quin, submit this Declaration to establish reduction to practice of the invention of the above-referenced patent application prior to November 28, 2000, which is the filing date of Provisional Patent Application Serial Number 60/253,959, to which U.S. Patent No. 6,875,176 claims priority. U.S. Patent No. 6,875,176 was granted to Mourad et al. and was cited in an Office Action dated March 13, 2007, in regard to a rejection of the pending claims in the above-referenced patent application.

I hereby declare that:

1. I am an inventor of the above-referenced patent application.
2. Exhibits A and B attached hereto are submitted as evidence of a date of reduction to practice of the invention of the above-referenced patent application prior to November 28, 2000, which is the earliest priority date to which U.S. Patent No.

6,875,176 to Mourad et al. could claim priority, via Provisional Patent Application Serial Number 60/253,959.

3. Exhibit A is a nine (9) page presentation that I developed prior to November of 2000.
4. Exhibit B is a four (4) page publicity piece making reference to work being performed in regard to my invention.
5. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statement may jeopardize the validity of the application or any patent issuing thereon.

Date: June 1, 2007



Yixian Qin

A Scanning Confocal Acoustic Diagnostic for Bone Quality

Vixian Qin

Biomedical Engineering

State University of New York at Stony Brook

Supported by Innovative Technology Grant

Background

- Osteoporosis - A leading cause of bone fractures
- 25 million people suffer from osteoporosis in the US alone
- 1.3 million fractures are attributed to osteoporosis annually
- Annual direct cost over 15 billion US dollars
- 1/3 of women over 65 have vertebral fractures
- 90% of women over 75 have X-ray evidence of osteoporosis

Current noninvasive diagnostic methods

- Dual energy X-ray absorptiometry (DEXA)
- Single and dual photon absorptiometry (SPA & DPA)
- Computerized tomography (CT)
- All based on X-ray



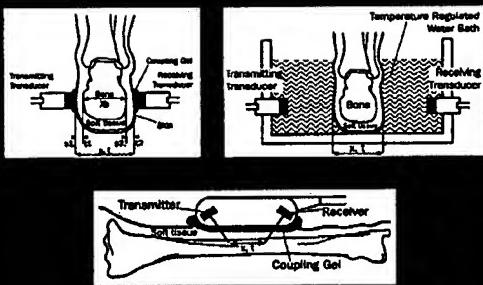
Current noninvasive diagnostic methods (cont.)

- DEXA is the best and most common tech in multi-sites, resolution and precision, but,
- In sensitive, certain bone must be lost before significance can be detected by DEXA
- Only provide an index with age risk
- Radiation and high cost (\$150k for machine alone)

Ultrasonic Techniques

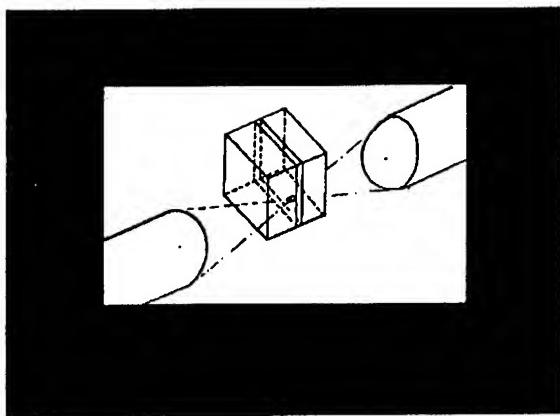
- Non-invasive
- Non-destructive
- Non-radiation
- Accurate

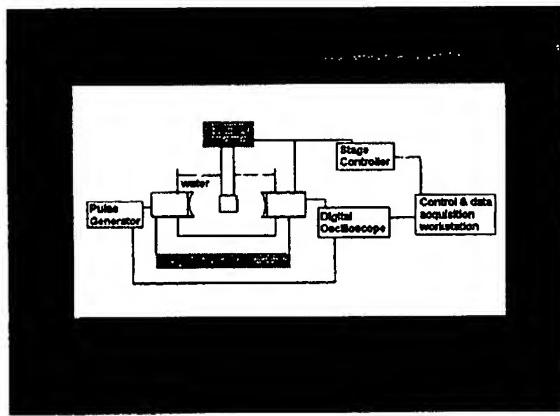
Ultrasonic waves are transmitted through a liquid medium (water bath) to a bone structure. The waves are reflected back to a receiver transducer.

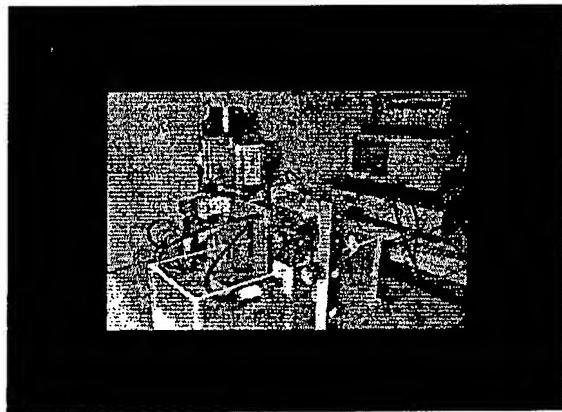


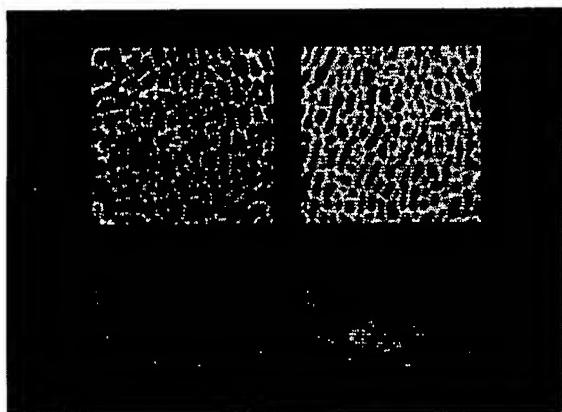


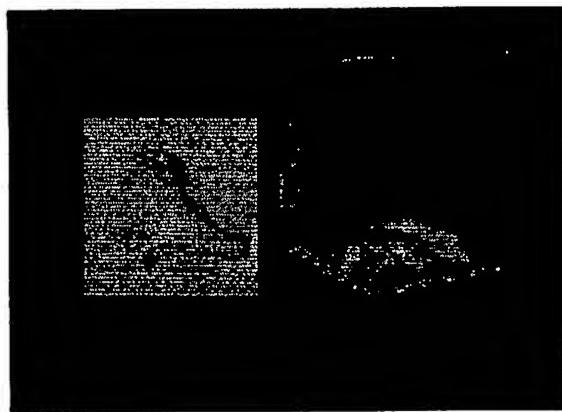
Architecture of osteoporotic bone

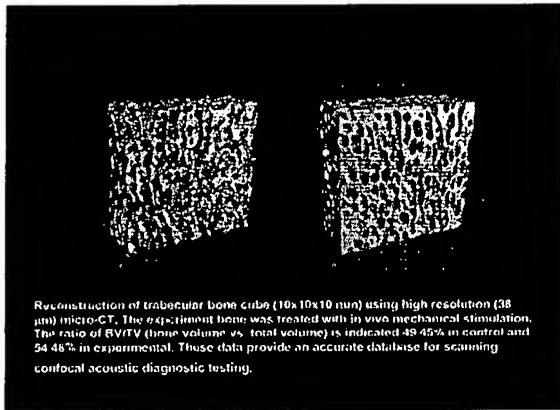
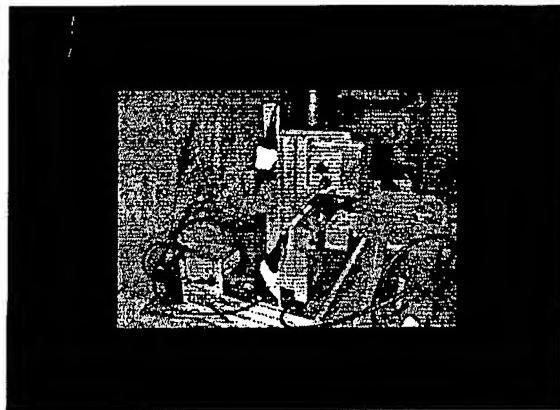




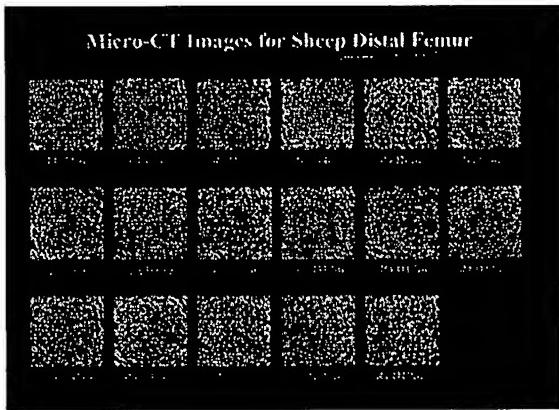


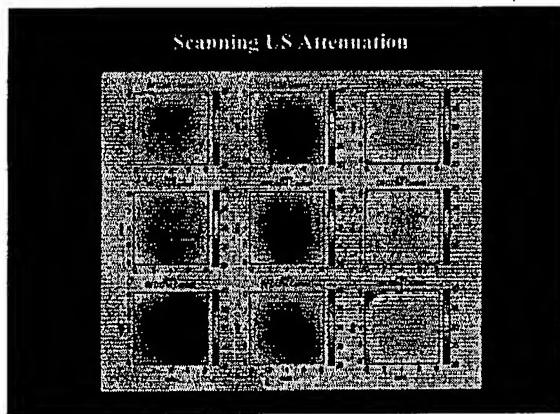


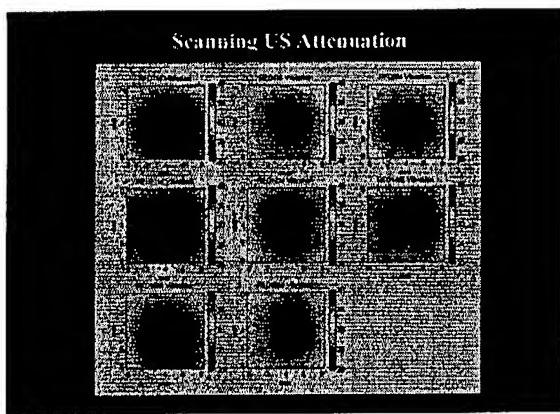


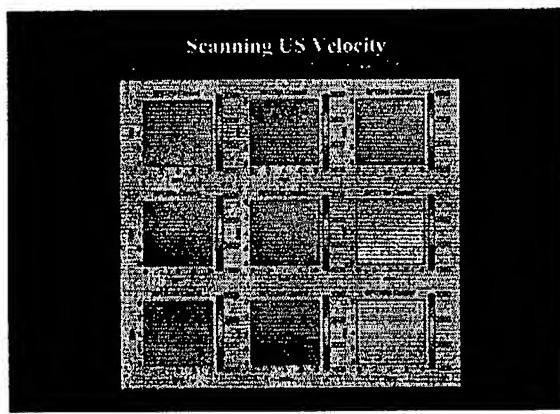


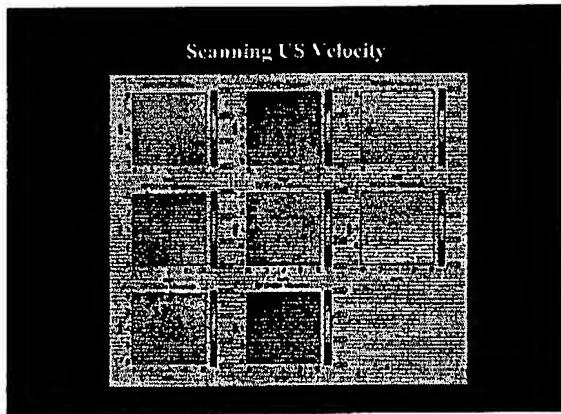
Reconstruction of trabecular bone cubes (10x10x10 mm) using high resolution (38 μ m) micro-CT. The experimental bone was treated with in vivo mechanical stimulation. The ratio of BV/TV (bone volume vs. total volume) is indicated 49.45% in control and 54.48% in experimental. These data provide an accurate database for scanning confocal acoustic diagnostic testing.

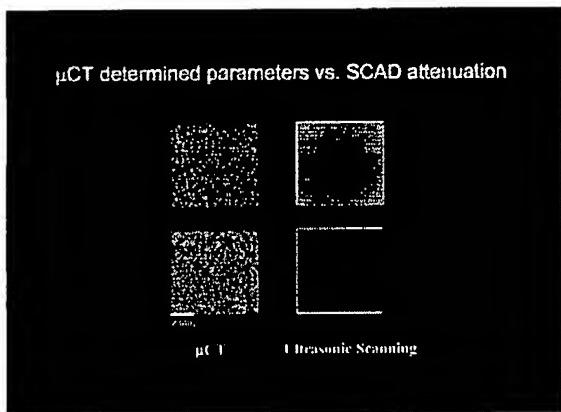


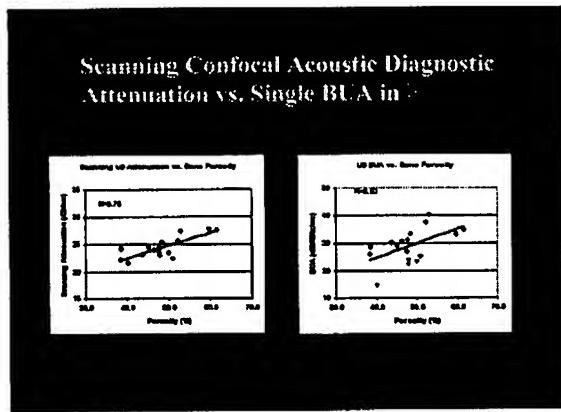


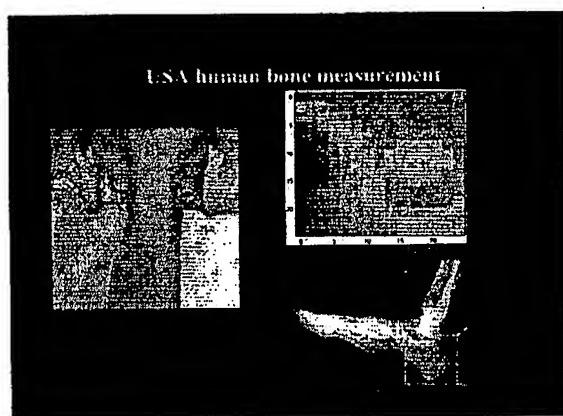
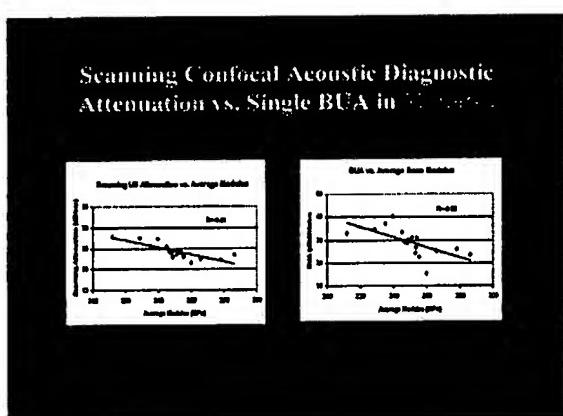
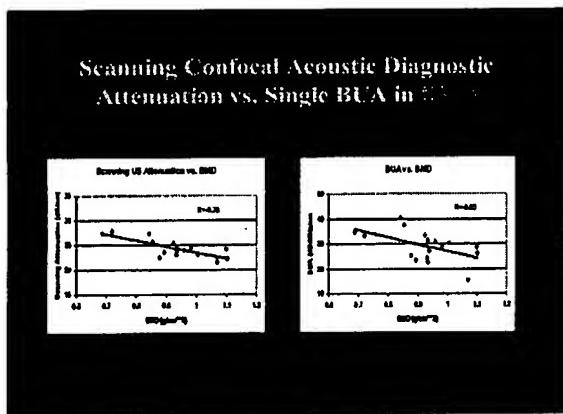












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Unique technology

- 1) Confocal ultrasonic technology to increase the spatial resolution and reduce noise.
- 2) Measuring both bone mineral density and bone strength.
- 3) Ultrasonic confocal point can be as fine as 0.1 mm, which is extremely useful.
- 4) 3-D scanning to identify bone quality in the region of interesting.
- 5) Fractal analysis of images determined by μ CT and ultrasound scanning, and determining their site-specific interrelationship and fractal coefficient.

Unique technology (cont.)

Determined bone quality coefficients

Bone Mineral Density index F_{BMD} :

$$F_{BMD}(\xi, \eta, \zeta) = \Psi(\xi, \eta, \zeta) \Lambda(\xi, \eta, \zeta),$$

Where Ψ is the coefficient parameter bridging the relation between ultrasound attenuation and BMD, ξ, η, ζ are the microstructural parameter determined by μ CT in porosity, BUC and trabecular width, respectively.

Bone strength index G_i :

$$G_i(\phi, \gamma, \lambda) = \Gamma(\phi, \gamma, \lambda) \rho V_i^2 \quad i = 1, 2, 3,$$

Where Γ is the coefficient parameter bridging the relation between ultrasound velocity and bone strength, ϕ, γ, λ are the microstructural parameter determined by μ CT, ρ is bone density, V is the ultrasonic velocity in three orthogonal directions.

Bone quality index II:

$$H(\mu, \gamma, \tau) = \Psi(\mu, \gamma, \tau) \Lambda(\mu, \gamma, \tau) + \Gamma(\mu, \gamma, \tau) \rho V^2$$

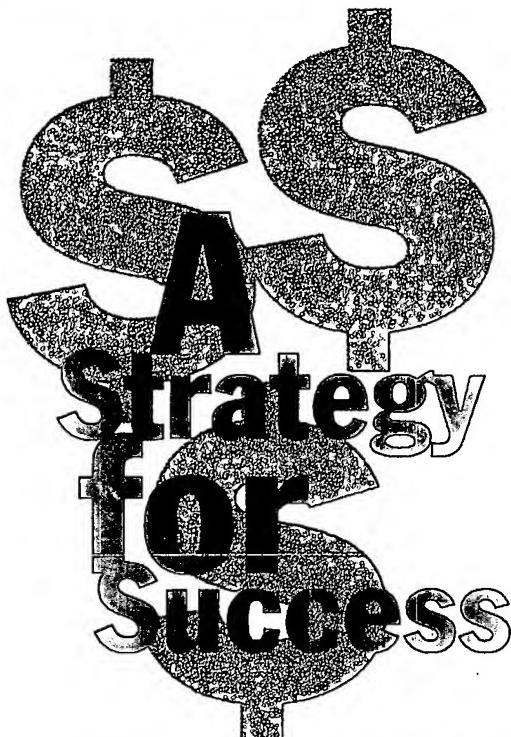
Where μ, γ, τ are the coefficients associated with μ CT and mechanical testing.

VENI, VIDI, INVENTI

A publication of the Center for Biotechnology

October/November, 2000

A New York State Center for Advanced Technology



Innovative Technology Development Program GOOD SCIENCE MAKES GOOD BUSINESS

Translating "good science into good business"... The Center for Biotechnology has been largely successful in fueling economic development in New York State by capitalizing on the tremendous resources inherent in the State's academic institutions. The Center's annual economic impact for fiscal year 1999-2000 alone is estimated at \$158M with 148 new jobs created.

A portion of the Center's success can be attributed to its unique Technology Development Initiative. The goals of the Initiative are to increase the number of income-producing technologies resulting from New York's research enterprise, while enhancing the financial value and return from these technologies by providing guidance and direct support in development toward commercial goals. The Initiative also aims to bundle synergistic technologies together to maximize value and to capture the economic benefit for New York State through the establishment of new companies and by out-licensing these "value-added" technologies to New York's bioscience industry.

The Center has begun to implement a winning formula for harnessing the enormous intellectual potential of New York State's academic institutions. A key component of

the Technology Development Initiative is the Innovative Technology Development (ITD) program which funds innovative, commercially promising, faculty research, alone or in partnership with industry. "No mechanism currently exists to adequately bridge the gap between discovery and early stage commercial development. As a result, a university's principal asset, its research, is often left undeveloped, its full commercial potential unrealized," states Clint Rubin, Director, Center for Biotechnology.

The ITD program aims to add value to technologies that will facilitate licensing, strategic partnerships, and/or new company formation. The Center fosters collaborative research and develops relationships with the biomedical industry as a means of accelerating discovery and development of technologies, and promoting faculty involvement with the bioscience industry sectors of New York State.

Through the ITD Program (formerly called the Innovative Technology Grant), the Center proactively identifies commercially promising technologies in New York State's academic institutions and systematically develops them for entry into the market. Unlike traditional models of technology transfer, research projects with commercial potential are nurtured by staff at the Center and developed beyond the initial concept stage. Corporate partners who license these technologies benefit from the reduced risk associated with the development of these more advanced technologies and from the accelerated product development cycle.

"Investment in basic research and the evolution of the biotechnology industry are inextricably linked. An investment in the discovery and development of commercially promising technologies within the academic environment will greatly increase the pool of income-producing technologies, yield greater returns, and generate new company formation," states Diane Fabel, Deputy Director, Center for Biotechnology.

Through the ITD program, the Center's Technology Development Initiative has already produced significant results. Four current-year ITD projects and two previously funded projects are under consideration for company formation. Two additional projects were co-sponsored by New York companies under the ITD program during the 1999/2000 fiscal year. In a collaboration between Roswell Park Cancer Institute and ZeptoMetrix (Buffalo, NY), DNA damage kits have been developed for research markets that have the potential to generate millions of dollars in revenue over the next five years. Vitex (Melville, NY), and SUNY Stony Brook are collaborating on the development of fibrin composites for treatment of severe wounds.

continued on page 2



The ITD program supports commercially promising research in all areas of medical biotechnology, including research products, diagnostics, medical devices, drug design, drug discovery, drug delivery, biomaterials, and biengineering. Faculty at New York State research institutions, alone or in partnership with a New York State company, are eligible to apply. Applications in the area of diagnosis or treatment of chronic disease and hereditary disorders; cardiovascular disease; inflammation; infectious disease; cancer; metastases; and research products with great commercial potential, are especially encouraged in this solicitation.

Objectives of the Program:

- Undertake high quality translational research with significant potential for economic payoff
- Stimulate technological innovation and new product development through university/industry collaborations
- Increase commercialization of university innovations through strategic industry partnerships or new company formation
- Maximize economic benefit to New York State
- Increase the value of intellectual property

The Center will give preference to projects which hold strong potential for commercialization within the near term (2-5 years) in New York State.

Application Procedure:

Faculty considering submission of a proposal are encouraged to contact Dr. Anil Dhundale, Director for Scientific Affairs (anil.dhundale@sunysb.edu). Application forms can be downloaded from the Center's web site at www.biotech.sunysb.edu, or by calling the Center at 631-632-6521.

The deadline for receipt of submitted proposals is 5 p.m., Friday, December 1, 2000. Late proposals and be accepted.



A Strategy for Success (continued from page II)

Projects supported in previous years are also beginning to fulfill their commercial potential as well. 3D Virtual Colonoscopy, a technology supported by the Center in 1996-1998, has lead to the formation of Viatronix (Stony Brook, NY), a company that will commercially exploit the medical applications of this imaging technology. Utilizing MRI and CAT scan data to create an image of a patient's colon, the technology allows doctors to non-invasively search for suspicious lesions. Functional Genetic Assay for Nuclear Import and Export, a research project supported by the Center (1997-2000), has resulted in a technology whose value has been greatly enhanced through the efforts of the Center's technology development staff. The technology is now available for license on a non-exclusive basis.

At least three Center-supported technologies are currently in human

clinical trials; a technology for the treatment of Dupuytren's Disease in partnership with Biospecifics Technologies Corp., (Lynbrook, NY); a technology for the early detection of cataracts; and a technology that uses polio recombinants as therapy for brain tumors.

Academic institutions will continue to play a significant role in the economic development of New York State. With the enactment of the J2K legislation, there is a recognition of the importance of strengthening the State's research infrastructure with the aim of fueling economic development in New York State. With this in mind, the Center will continue to develop its Technology Development Initiative to further bridge the intellectual wealth of New York State's academic institutions to the bioscience industry.

UNIQUE DIAGNOSTIC TOOL FOR USE IN OSTEOPOROSIS RESEARCH

Center funds SUNY Stony Brook project that uses ultrasound to detect bone quality

Dr. Yi-Xian Qin, from the Program in Biomedical Engineering at Stony Brook University, is working on a project entitled, "A Scanning Confocal Acoustic Diagnostic (SCAD) for Bone Quality." This project is focused on developing a system that will be capable of detecting bone mass and quality using ultrasonic attenuation and velocity scanning. Techniques that utilize ultrasound provide an intriguing method for characterizing the material properties of bone in a manner that is non-invasive, non-destructive, and relatively accurate. Dr. Qin states, "The primary advantage of ultrasound, as applied with this technology, is that it allows for the measurement of not only bone density, but also bone quality."

SCAD will offer clinicians a diagnostic tool to determine the bone quality of patients suffering from various musculo-skeletal disorders, such as osteoporosis. Osteoporosis is a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased susceptibility to fractures of the hip, spine, and wrist. According to the National Osteoporosis Foundation, 25 million Americans are currently afflicted with osteoporosis and 18 million are at risk because of low bone density. Studies estimate that as many as 1.5 million fractures occur each year due to an osteoporosis condition. This data becomes even more significant after considering the U.S. Census Bureau study, "Data Base News in Aging," because the report indicates that the current elderly population (ages 55-85+) amounts to 21.5 million. Moreover, the baby boom generation, which includes only those between 35-55 years, amounts to an astounding 39 million people. Based on these data, the current trends of age-related health risks, such as osteoporosis, will increase dramatically throughout the next century.

Several potential commercialization strategies can be derived from Dr. Qin's technology, including licensing the intellectual property to an existing firm that may be interested in further development, or through the formation of a start-up corporation aimed at capitalizing on the market potential and competitive advantages of the technology. The Center is working closely with Dr. Qin and the Office of Technology Licensing to determine an appropriate development path. Dr. Qin states, "We are very excited about the commercialization opportunities, and the Center has been very helpful in moving this technology forward."

Companies interested in learning more about the potential of this technology should contact Rob Shorr, Director, Business Development, at the Center for Biotechnology at 631-632-8521.

INDUSTRY PARTNERSHIPS

TECHNOLOGY

Antisense Technology

Intervenes at the genetic level making it theoretically possible to address any disease caused by the malfunction of a gene.

CORPORATE PARTNER

Enzo Biochem

Antibody to Prevent Platelet Aggregation and Restinosis of Coronary Arteries

Inhibits fibrinogen attachment thereby preventing platelet aggregation.

Centecor/Eli Lilly

Modified Tetracycline Technology

Inhibits destruction of collagen with applications in the treatment of periodontal disease, cancer, osteoporosis, and osteoarthritis.

Collagenex

Biomaterial Applications of Hyaluronic Acid

HA has been chemically modified to produce novel biomaterials for drug-delivery and tissue engineering.

Clear Solutions Biotech

Genetic System to Detect Protein-Protein Interaction

Identifies the gene for an interactive protein of interest.

45+ companies worldwide

Improved Diagnosis of Lyme Borreliosis

Provides a major breakthrough in the sensitivity and accuracy in the diagnosis of Lyme disease.

Brook Biotechnology

Rapid Diagnostic Assay for Detecting Helicobacter pylori

A system for detecting the presence of *H. pylori* in gastric juice by measuring ammonia concentration.

Enteric Products

Low level Biomedical Prophylaxis for the Inhibition of Osteopenia

Use of extremely low strain magnitudes at relatively high frequencies, to reverse the bone loss in aging.

Exogen

3D Virtual Colonoscopy

A non-invasive cancer screening device that helps clinicians identify suspicious lesions.

Viatronix

Bioengineering and Biotechnology Seminar Series, 2000-2001

4:00pm on Wednesday Afternoons, Atkins Learning Center, 4th Floor, Health Sciences Center SUNY Stony Brook

September 13, 2000

**Organization of Bone and Other Mineralized Tissues:
Insight into Mechanism of Biological Mineralization**
Melvin Glimcher, M.D.
Harriet M. Peabody Professor of Orthopaedic Surgery
Harvard Medical School, Boston, MA

October 18, 2000

**cDNA Microarrays; The Opportunities and
Challenges of a New Genomics Technology**
Anil Dhundale, Ph.D.
Director of Scientific Affairs, Center for Biotechnology
State University of New York at Stony Brook

November 15, 2000

**From Benchtop to Bedside; The Travails of
Bringing Bone Morphogenic Protein to the Clinic**
Howard Seherman, Ph.D., V.M.D.
Senior Scientist
Genetics Institute, Cambridge, MA

December 13, 2000

The Early Response in Functional MRI
Thomas Ernst, Ph.D.
Director of Medical Physics
Brookhaven National Laboratory, Upton, NY

February 14, 2001

Tissue Engineering of the Musculoskeletal System
Rocky S. Tuan, Ph.D.
Professor of Orthopaedic Surgery, Biochemistry
& Molecular Pharmacology
Thomas Jefferson University, Philadelphia, PA

March 14, 2001

Engineering of Cardiovascular Tissues
Robert M. Nerem, Ph.D.
Professor and Director
Parker H. Petit Institute for Bioengineering and Bioscience
Georgia Institute of Technology

April 11, 2001

**High Speed Genomic Sequencing: A Unique
Approach to Improved Sensitivity**
Vera Gorinikel, Ph.D.
Associate Professor of Electrical Engineering
State University of New York at Stony Brook

May 9, 2001

**Molecular Mechanisms of Fracture Healing:
Can Intervention Improve on Mother Nature?**
Mark Bolander, M.D.
Professor of Orthopaedic Surgery, Mayo Clinic, Rochester, MN

For further information, please contact: The Program in Biomedical Engineering at 631-632-2302

Veni, Vidi, Inveni, a publication of the Center for Biotechnology, is published quarterly. We welcome comments, suggestions and submissions.

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